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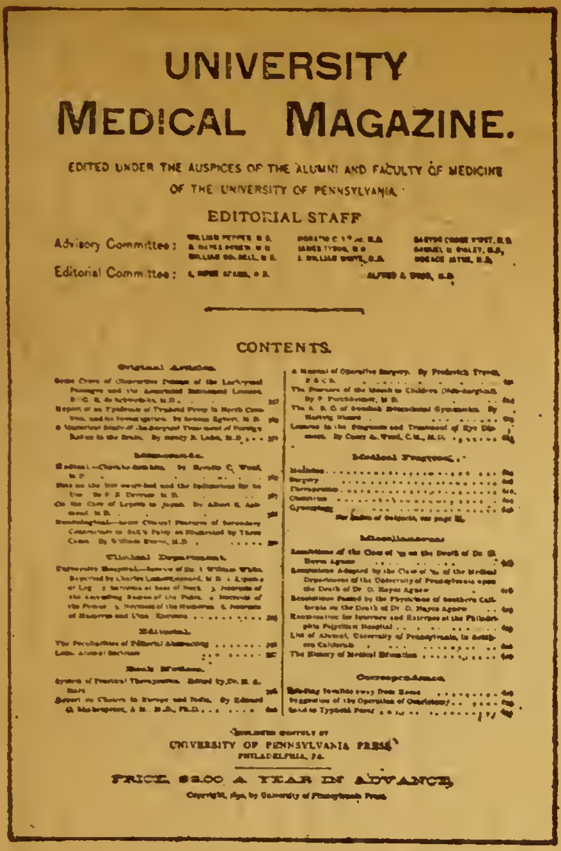

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STRONTIUM SALICYLATE.

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Professor of Therapeutics in the University of Pennsylvania.

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The medical world everywhere recognizes that the salicylates are valuable in the treatment of rheumatic and gouty affections, and that their usefulness is often interfered with by the great tendency which they have to derange digestion. In common, I suppose, with most practitioners of medicine, for some years I have been trying to find some way of getting the general action of the salicylates without gastric disturbance. At one time most of my patients received oil of gaultheria, which certainly in many cases is less disturbing to the gastric mucous membrane than is the salicylic acid or the sodium salicylate. Subsequently, however, I found that the ammonium salicylate, given in milk, was usually much better borne than was even the oil of gaultheria. In the earlier editions of my Treatise on Therapeutics it was recommended to dissolve salicylic acid in water by the cautious addition of ammonia, but this crude method of preparing ammonium salicylate was in turn replaced by the use of the ammonium salicylate as made by the manufacturing chemist. In Philadelphia at least, and presumably in other places, the ammonium salicylate has come largely into use. It is a freely soluble salt, which is rapidly absorbed, and rapidly produces, when given in sufficient amount, the cinchonism that marks the salicylic action. Strangely enough, it was not only not made official in the late revisions of the British and United States Pharmacopeias, but is not even mentioned in the recent editions of the United States Dispensatory, nor in the new National Dispensatory; an omission which is the more strange, at least so far as the United States Dispensatory is concerned, because I daily prescribe the salt. Hith-

erto it has certainly offered the best method of administering the salicylates for ordinary purposes, and I believe that when an immediate powerful impression is desired, it still remains the best remedy of its class.

My own clinical experiments closely accord with the statements of Laborde, that the haloid strontium salts agree with the human digestive apparatus very much better than do the corresponding salts of sodium and potassium; and it occurred to me that very possibly the strontium might be able to overcome the disagreeable effects of salicylic acid. At my request, Rosengarten & Sons, manufacturing chemists, very kindly prepared for me the salt, which occurs in an irregularly, coarsely crystalline powder, or, as it was furnished to me by the chemists, finely pulverized. According to the determination of Professor Wormley, it is soluble in 31.25 parts of cold water, but by means of heat a permanent 6-per-cent. solution can be made. In the proportion of its salicylic acid it compares with the sodium salicylate as 1.4 does to 1 (161 parts of sodium salicylate equalling 138 parts of salicylic acid).

When given intravenously in fatal dose to the dog it produces death through the respiration, followed almost at once by an extraordinary post-mortem rigidity. In some instances there was vomiting, but never purging.

In order to determine whether it has any distinct depressing influence on the circulation, experiments upon dogs were made with it; and also, for control, with the sodium and ammonium salicylate.

Experiment I.—Dog, weighing 28.6 kilos *Sodium salicylate*, 6-per-cent. solution. The arterial pressure was not distinctly affected by the intravenous injection of 100 cubic centimetres; after 40 cubic centimetres more there was a rise of 10 millimetres in the arterial pressure, which was maintained for between one and two minutes, when under the influence of another 20 cubic centimetres the pressure began to fall slowly. Another 20 cubic centimetres being given the rate of fall was increased; when the arterial pressure had decreased from 180, the norm, to 52 millimetres, the respiration ceased; the heart continuing to beat for half a minute longer.

Experiment II.—Dog, weighing 21.4 kilos. *Ammonium salicylate*, 6-per-cent. solution. The rapid injection of 20 cubic centimetres of the solution into the jugular was followed by a pronounced immediate fall of pressure followed in a few seconds by a rise; after repetition until 80 cubic centimetres had been injected the pressure rose to 20 millimetres above the norm. This rise was increased 16 millimetres by the further gradual injection of 80 cubic centimetres of the solution. During the very slow injection of 40 cubic centimetres more the

pressure remained about the same until the whole had been given, when violent tetanus developed, and the arterial pressure rose to 56 millimetres above the norm, only to rapidly fall a half minute later, when the muscles relaxed during quiet to 112 millimetres below the norm. Ten seconds after this respiration ceased, the heart continuing to beat for twenty seconds, and the arterial pressure gradually descending to zero.

A study of these experiments will show that with the sodium salicylate there was a slight rise of pressure, which was followed by a fall when 5 6 cubic centimetres of the solution per kilo. had been injected; with the ammonium salicylate a great rise of pressure occurred, followed by a fall when the injected solution amounted to 9.5 cubic centimetres per kilo. A study of these results brings into relief the stimulating influence of the ammonia in contrast with the inertness of the soda. It is evident that in the salicylates the physiological properties of the base are not without influence upon the paralyzing action of the toxic dose of the salicylic acid.

As I am not aware that any experiments of the strontium salicylate upon the circulation have been made, I record two experiments in greater detail than those just given.

Experiment. Dog; weight, 20 kilos.; 3-per-cent. solution of the strontium salicylate, given by intravenous injection into the jugular.

Time. h. m.	Dose.	Pulse.	Pressure.	Remarks.
0.	. . . . . .	220	128–138	
0.1	10 c.c.	. . .	. . . . . .	
0.30	10 "	. . .	. . . . . .	
0.40	. . . . . .	204	130–150	
1.40	10 c.c.	. . .	. . . . . .	
1.55	. . . . . .	. . .	130–150	
3.00	20 c.c.	. . .	. . . . . .	
3.55	. . . . . .	. . .	130–140	
5.00	30 c.c.	. . .	. . . . . .	
5.40	. . . . . .	. . .	130–140	
6.00	10 c.c.	. . .	. . . . . .	
6.10	10 "	60	130–160	Pulse suddenly altered in character.
6.25	20 "	. . .	. . . . . .	
6.35	. . . . . .	. . .	140–175	
7.05	. . . . . .	. . .	140–200	Dog vomiting.
7.15	. . . . . .	. . .	140–260	Dog vomiting.
7.30	30 c.c.	. . .	. . . . . .	
7.55	. . . . . .	. . .	150–190	
8.05	10 c.c.	. . .	. . . . . .	
8.10	. . . . . .	. . .	150–180	
8.25	10 c.c.	. . .	. . . . . .	
9.25	. . . . . .	. . .	160–170	
10.25	10 c.c.	. . .	. . . . . .	
12.25	. . . . . .	. . .	150–160	
20.25	. . . . . .	. . .	150–160	Dog quiet.

EXPERIMENT, November 17, 1894. Dog; weight, 13.152 kilos.; 6-per-cent. solution of the strontium salicylate used.

Time. h. m. s.	Dose.	Pulse.	Pressure.	Remarks.
4.14	. . . .	27	146	
4.15.10 to 40	20 c.c.	. . .	. . . . . .	
4.15.20	. . . .	. . .	164	Struggling.
4.15.40	. . . .	. . .	152	
4.16	. . . . .	. . .	166	Struggling.
4.18	. . . .	19	150	Quiet.
4.19	. . . .	19	144	
4.19.10 to 25	20 c.c.	. . .	. . . . . .	
4.19.30	. . . .	. . .	166	Struggling.
4.20	. . . .	. . .	162	Struggling continues.
4.21.30	. . . . .	20	154	Slight struggling.
4.22.4to22.20	20 c.c.	. . .	. . . . . .	Quiet.
4.22.20	. . . .	. . .	166	Struggling.
4.23.30	. . . .	. . .	148	
4.23.30 to 40	10 c.c.	. . .	. . . . . .	
4.23.50	. . . .	. . .	. . . . . .	Continuous struggling.
4.24	. . . .	. . .	158	
4.24.4to24.20	10 c.c.	. . .	. . . . . .	
4.24.30	. . . .	. . .	172	
4.25	. . . .	23	170	Quiet.
4.25 4to25.10	10 c.c.	. . .	. . . . . .	
4.27.30	. . . .	. . .	156	
4.27.40 to 50	10 c.c.	. . .	. . . . . .	
4.28	. . . .	. . .	166	
4.28.4to28.10	10 c.c.	24	164	Struggling.
4.29.4to29.10	10 c.c.	. . .	162	
4.29.20	. . . .	. . .	158	Struggling.
4.29.30 to 40	10 c.c.	. . .	158	
4.30	. . . .	35	160	Slight struggling.
4.30.4to30.10	10 c.c.	. . .	. . . . . .	
4.30.20	. . . .	. . .	160	Struggling.
4.30.30	. . . .	. . .	154	
4.30.40 to 50	10 c.c.	. . .	. . . . . .	
4.31	. . . .	. . .	134	Struggling.
4.31.30	. . . .	. . .	118	
4.32	. . . .	. . .	108	Struggling.
4.33	. . . .	. . .	98	
4.33.30	. . . .	. . .	52	
4.33.40	. . . .	. . .	. . . . . .	Respiration stopped. Heart continued twenty seconds (to 4.34).

In examining the records it will be seen that in the first experiment 210 cubic centimetres of a 3-per-cent.solution, equal to 105 cubic centimetres of a 6-per-cent. solution, increased the arterial pressure markedly in a dog weighing 20 kilos.; so that over 5 cubic centimetres of a 6-per-cent. solution of strontium salicylate per kilo., intravenously injected, raised the blood-pressure 22 millimetres.

In the second experiment, after the injection of 150 cubic centimetres of a 6-per cent. solution of strontium salicylate in a dog weighing 13 kilos., the blood-pressure was still above the norm; although a few seconds later an additional injection of 10 cubic centimetres was followed by rapid fall of pressure, ending in death by respiratoy arrest;

the heart continuing to beat distinctly twenty seconds after respiration had stopped. In other words, 11 cubic centimetres per kilo. of a 6-per-cent. solution of the strontium salicylate intravenously injected in broken doses for a length of time did not produce any immediate fall of pressure.

Contrasting these results with those obtained with sodium and ammonium, it will be seen that the dose of the strontium salicylate necessary to lower arterial pressure was nearly twice that of the sodium salicylate, and distinctly more than that of the ammonium salicylate.

With the knowledge acquired by animal experimentation it seemed to me entirely safe to use the strontium salicylate in human medicine, and I have accordingly employed it in a large number of cases in doses of from 15 to 120 grains a day. The result of these trials is to show that in doses of 5 to 10 grains, given after meals, the salt very commonly improves digestion, and in the dose of five grains an hour after meals, in flatulent dyspepsia and various conditions of tendency to fermentative changes in the alimentary canal, it is a useful intestinal antiseptic, which has seemed to me to give better results than do salol, naphthol, or other of the older intestinal antiseptic remedies. It does not produce cinchonism as readily as do the older salicylates, but it is entirely capable of causing a pronounced degree of cinchonism. I have not been able to test it in acute articular rheumatism, but it would probably be less efficacious than the ammonium salicylate. In muscular or subacute rheumatism as well as in chronic gouty conditions with a tendency to digestive disturbance, I have found it to be a very valuable remedy, exerting the action of the salicylate upon the diathesis, and improving instead of injuring the digestion. It may be given in solution, but is best administered in capsules ; a five-grain capsule is of moderate size, and of these two or more may be taken at once. It is probable that it would be well administered in compressed tablets, but in this way I have not tested it. The taste of this salt is similar to but distinctly less offensive than that of the ordinary salicylates, so that if preferred it may be given in weak solution.